

WHAT IS CLAIMED IS:

1. A method for treating inflammatory bowel disease in a patient comprising administering to said patient a sustained release pharmaceutical composition comprising a pharmaceutically effective amount of an anti-malarial compound in association with a pharmaceutically acceptable excipient which delays and targets the release of said anti-malarial compound in the gastrointestinal tract of the patient.

2. The method according to Claim 1 wherein the inflammatory bowel disease is Crohn's disease.

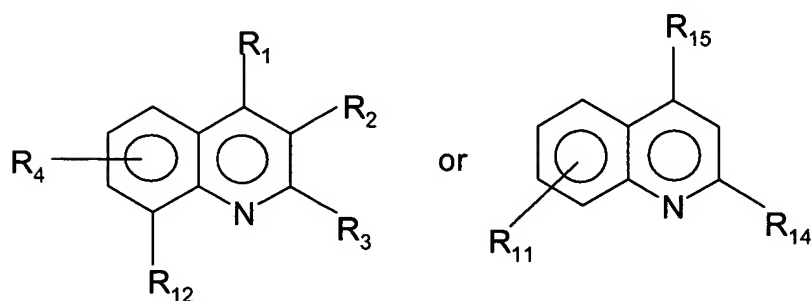
3. The method according to Claim 1 wherein the inflammatory bowel disease is ulcerative colitis.

4. The method according to Claim 1 wherein the inflammatory bowel disease is indeterminate colitis.

5. The method according to Claim 1 wherein the inflammatory bowel disease is infectious colitis.

6. The method according to Claim 1 wherein the anti-malarial compound is aminoquinoline or hydroxyquinoline.

7. The method according to Claim 6 wherein said aminoquinoline has the formula:



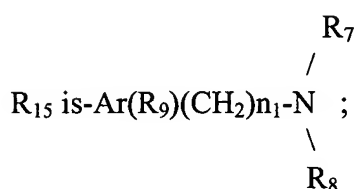
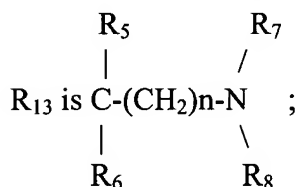
or pharmaceutically acceptable salts thereof,

wherein

R₂ and R₃ are independently hydrogen, or lower alkyl or R₂ and R₃ taken together with the carbon atoms to which they are attached form an aryl ring, which aryl

ring is unsubstituted or substituted with an electron withdrawing group or an electron donating group,

one of R_1 and R_{12} is NHR_{13} while the other is hydrogen;



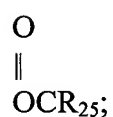
R_4 , R_{10} , R_{11} and R_{14} are independently hydrogen or an electron donating group or electron withdrawing group;

R_5 and R_6 , are independently hydrogen or lower alkyl which may be unsubstituted or substituted with an electron withdrawing or electron donating group;

R_7 and R_8 are independently hydrogen or lower alkyl, which may be unsubstituted or substituted with an electron withdrawing or electron donating group;

Ar is aryl having 6-18 ring carbon atoms which may be unsubstituted or substituted with an electron donating or electron withdrawing group;

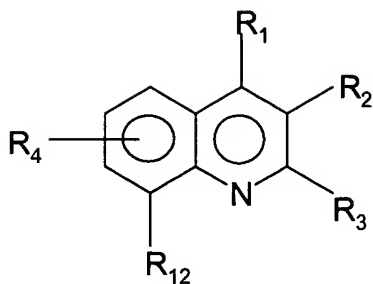
R_9 is hydrogen or hydroxy or lower alkoxy or



R_{25} is lower alkyl or hydrogen; and

n and n_1 are independently 1-6.

8. The method according to Claim 7 wherein the aminoquinoline is of the formula:



9. The method according to Claim 8 wherein R₁ is NHR₁₃ and R₁₂ is hydrogen.
10. The method according to Claim 9 wherein R₅ is hydrogen and R₆ is lower alkyl.
11. The method according to Claim 9 wherein R₅ is hydrogen and R₆ is methyl.
12. The method according to Claim 9 wherein n is 3.
13. The method according to Claim 9 wherein R₃ is hydrogen.
14. The method according to Claim 9 wherein R₄ is substituted in the 7-position of the quinoline ring.
15. The method according to Claim 11 wherein R₄ is 7-halo.
16. The method according to Claim 15 wherein halo is chloro.
17. The method according to Claim 9 wherein R₇ is ethyl and R₈ is ethyl or 2-hydroxy ethyl.
18. The method according to Claim 8 wherein R₁₂ is NHR₁₃ and R₁ is hydrogen.
19. The method according to Claim 18 wherein R₅ is hydrogen and R₆ is lower alkyl.
20. The method according to Claim 19 wherein R₅ is hydrogen and R₆ is methyl.
21. The method according to Claim 18 wherein n is 3.
22. The method according to Claim 19 wherein R₇ is hydrogen, methyl or ethyl and R₈ is hydrogen, methyl, ethyl, propyl

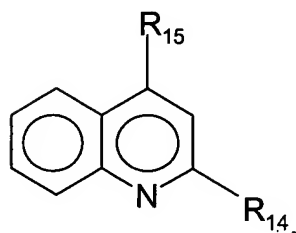
or isopropyl.

23. The method according to Claim 18 wherein R_4 is substituted on the 6-position of the quinoline ring.

24. The method according to Claim 23 wherein R_4 is 6-lower alkoxy.

25. The method according to Claim 24 wherein R_4 is 6-methoxy.

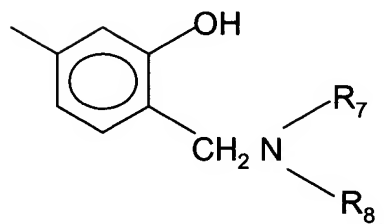
26. The method according to Claim 7 wherein the amino quinoline has the formula:



27. The method according to Claim 26 wherein Ar is phenyl.

28. The method according to Claim 26 wherein R_9 is hydroxy.

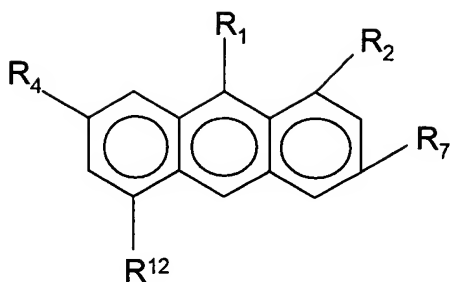
29. The method according to Claim 26 wherein R_{15} is



30. The method according to Claim 26 wherein R_7 and R_8 are independently lower alkyl.

31. The method according to Claim 30 wherein R_7 and R_8 are both ethyl

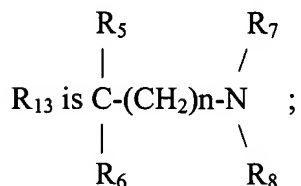
32. The method according to Claim 1 wherein the anti-malarial compound has the formula:



wherein

R_2 is hydrogen or lower alkyl;

one of R_1 and R_{12} is NHR_{13} while the other is hydrogen;



R_4 is hydrogen or an electron donating group or electron withdrawing group;

R_5 and R_6 , are independently hydrogen or lower alkyl which may be unsubstituted or substituted with an electron withdrawing or electron donating group;

R_7 and R_8 are independently hydrogen or lower alkyl, which may be unsubstituted or substituted with an electron withdrawing or electron donating group; and

n is independently 1-6.

33. The method according to Claim 1 wherein the anti-malarial agent is pomaquine, primaquine, pentaquinine, isopentaquine, quinacrine salt, chloroquine, hydroxychloroquine, ontoquine, amodiaquine, mefloquine, or mepacrine or pharmaceutically acceptable salts thereof.

34. The method according to Claim 1 wherein the anti-malarial compound is hydroxychloroquine, chloroquine, mepacrine, mefloquine, or

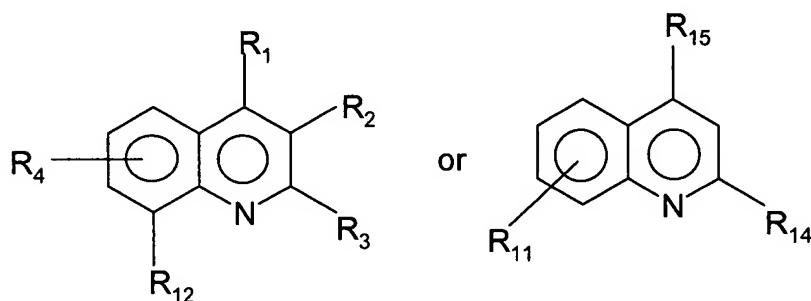
pharmaceutically acceptable salts thereof.

35. The method according to Claim 1 wherein the anti-malarial compound is hydroxychloroquine or a pharmaceutically acceptable salt thereof.

36. A pharmaceutical composition comprising a pharmaceutically effective amount of an anti-malarial compound in association with a pharmaceutically acceptable excipient which delays and targets the release of said anti-malarial compound in the gastrointestinal tract.

37. The pharmaceutical composition according to Claim 36 wherein the anti-malarial compound is aminoquinoline or hydroxyquinoline.

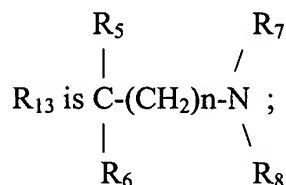
38. The pharmaceutical composition according to Claim 37 wherein said aminoquinoline has the formula:

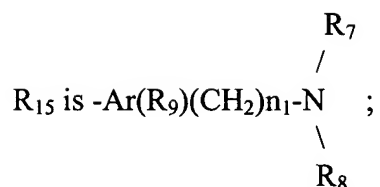


or pharmaceutically acceptable salts thereof,
 wherein

R₂ and R₃ are independently hydrogen, or lower alkyl or R₂ and R₃ taken together with the carbon atoms to which they are attached form an aryl ring, which aryl ring is unsubstituted or substituted with an electron withdrawing group or an electron donating group,

one of R₁ and R₁₂ is NHR₁₃ while the other is hydrogen;





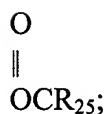
R_4 , R_{10} , R_{11} and R_{14} are independently hydrogen or an electron donating group or electron withdrawing group;

R_5 and R_6 , are independently hydrogen or lower alkyl which may be unsubstituted or substituted with an electron withdrawing or electron donating group;

R_7 and R_8 are independently hydrogen or lower alkyl, which may be unsubstituted or substituted with an electron withdrawing or electron donating group;

Ar is aryl having 6-18 ring carbon atoms which may be unsubstituted or substituted with an electron donating or electron withdrawing group;

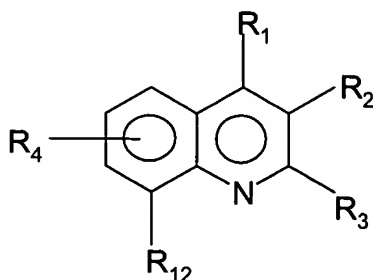
R_9 is hydrogen or hydroxy or lower alkoxy or



R_{25} is lower alkyl or hydrogen; and

n and n_1 are independently 1-6.

39. The pharmaceutical composition according to Claim 38 wherein the aminoquinoline is of the formula:



40. The method according to Claim 39 wherein R_1 is NHR_{13} and R_{12} is

hydrogen.

41. The method according to Claim 40 wherein R_5 is hydrogen and R_6 is lower alkyl.

42. The method according to Claim 40 wherein R_5 is hydrogen and R_6 is methyl.

43. The method according to Claim 40 wherein n is 3.

44. The method according to Claim 40 wherein R_3 is hydrogen.

45. The method according to Claim 40 wherein R_4 is substituted in the 7-position of the quinoline ring.

46. The method according to Claim 40 wherein R_4 is 7-halo.

47. The pharmaceutical composition according to Claim 46 wherein halo is chloro.

48. The pharmaceutical composition according to Claim 40 wherein R_7 is ethyl and R_8 is ethyl or 2-hydroxy ethyl.

49. The pharmaceutical composition according to Claim 39 wherein R_{12} is NHR_{13} and R_1 is hydrogen.

50. The pharmaceutical composition according to Claim 49 wherein R_5 is hydrogen and R_6 is lower alkyl.

51. The pharmaceutical composition according to Claim 50 wherein R_5 is hydrogen and R_6 is methyl.

52. The pharmaceutical composition according to Claim 49 wherein n is 3.

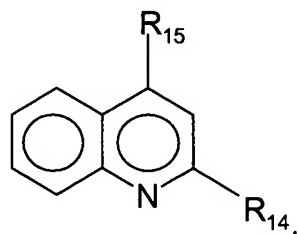
53. The pharmaceutical composition according to Claim 50 wherein R_7 is hydrogen, methyl or ethyl and R_8 is hydrogen, methyl, ethyl, propyl or isopropyl.

54. The pharmaceutical composition according to Claim 49 wherein R_4 is substituted on the 6-position of the quinoline ring.

55. The pharmaceutical composition according to Claim 54 wherein R_4 is 6-lower alkoxy.

56. The pharmaceutical composition according to Claim 55 wherein R_4 is 6-methoxy.

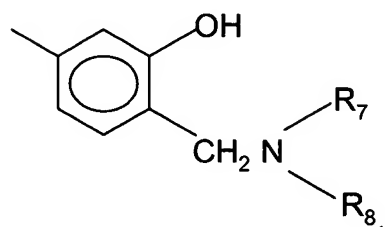
57. The pharmaceutical composition according to Claim 38 wherein the amino quinoline has the formula:



58. The pharmaceutical composition according to Claim 57 wherein Ar is phenyl.

59. The pharmaceutical composition according to Claim 57 wherein R_9 is hydroxy.

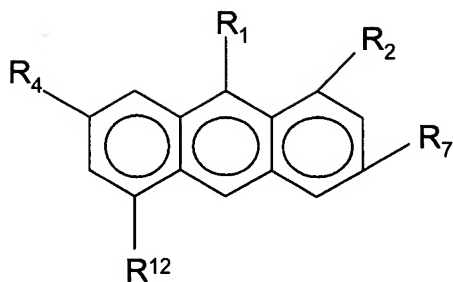
60. The pharmaceutical composition according to Claim 57 wherein R_{15} is



61. The pharmaceutical composition according to Claim 57 wherein R_7 and R_8 are independently lower alkyl.

62. The pharmaceutical composition according to Claim 61 wherein R_7 and R_8 are both ethyl

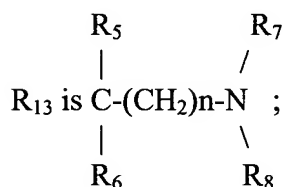
63. The pharmaceutical composition according to Claim 36 wherein the anti-malarial compound has the formula:



wherein

R_2 is hydrogen or lower alkyl;

one of R_1 and R_{12} is NHR_{13} while the other is hydrogen;



R_4 is hydrogen or an electron donating group or electron withdrawing group;

R_5 and R_6 , are independently hydrogen or lower alkyl which may be unsubstituted or substituted with an electron withdrawing or electron donating group;

R_7 and R_8 are independently hydrogen or lower alkyl, which may be unsubstituted or substituted with an electron withdrawing or electron donating group; and

n is independently 1-6.

64. The pharmaceutical composition according to Claim 36 wherein the anti-malarial agent is pomaquine, primaquine, pentaquinine, isopentaquine, quinacrine salt, chloroquine, hydroxychloroquine, sontoquine, amodiaquine, mefloquine, or mepacrine or pharmaceutically acceptable salts thereof.

65. The pharmaceutical composition according to Claim 36 wherein the anti-malarial compound is hydroxychloroquine, chloroquine, mepacrine, mefloquine, or pharmaceutically acceptable salts thereof.

66. The pharmaceutical composition according to Claim 36 wherein the anti-malarial compound is hydroxychloroquine or a pharmaceutically acceptable salt thereof.

67. The method according to Claim 1 wherein the inflammatory bowel disease is eosinophilic gastroenteritis.

68. The method according to Claim 2 wherein the Crohn's disease is characterized by eosinophila and selected from the group consisting of esophagitis, ileocolitis, jejunoileitis, colitis, perianal disease, proctosigmoiditis, and gastroduodenal Crohn's disease.

69. The method according to Claim 3 wherein the ulcerative colitis is characterized by eosinophila and selected from the group consisting of ileitis, proctosigmoiditis, and proctitis.

70. A method of preventing or treating an inflammatory bowel disease characterized by eosinophilia comprising:

measuring an eosinophil count of a patient in determining the need for treatment of a disease characterized by eosinophila and selected from the group consisting of eosinophila caused by ulcerative colitis, eosinophilic gastroenteritis, Crohn's disease, esophagitis, ileitis, proctosigmoiditis, and proctitis; and

administering a pharmaceutically effective amount of an anti-malarial compound to a patient in need thereof to suppress eosinophilia.